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Numerical Modeling of Renal Ionic Equilibrium for Implantable Kidney Applications

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Abstract:

The human kidney is one of the most important organs in the human body; it performs many functions and has a great impact on the work of the rest of the organs. Among the most important possible treatments is dialysis, which works as an external artificial kidney, and several studies have worked to enhance the mechanism of dialysate flow and improve the permeability of its membrane. This study introduces a new numerical model based on previous research discussing the variations in the concentrations of sodium, potassium, and urea in the extracellular area in the blood during hemodialysis. We simulated the differential equations related to mass transfer diffusion and we developed the model in MATLAB Simulink environment. A value of 700 was appeared to be the most appropriate as a mass transfer coefficient leading to the best permeability. The suggested models enabled to track the temporal variations of urine, K and Na concentrations in blood streamline. This also produced the time needed to reach the requested concentrations mentioned in literature studies (960 ms). Concentrations evaluation was performed with error rates not exceeding 2% for all ions compared to the normal values of human blood.The current work presents the first step towards combinig the mass transfer and diffusion principles with our efforts in designing and implementing an electrophoresis-based implantable kidney.

Key words: Applications of implantable kidney, Kidney design, Matlab, Numerical modeling, Renal ions equilibrium.

Introduction:

Chronic kidney diseases are increasing worldwide with about 10% of the world's adult population. Although it affects all age groups and gender, it is more prevalent among elderly individuals, where the prevalence rate among people over 64 years of age ranges between 3-36% [1]. Chronic kidney diseases are defined as a decrease in the glomerular filtration rate to less than 60 mL /min per 1.73 m^2 or signs of kidney damage, often identified by albuminuria, for more than 3 months [2]. Recent studies have indicated that kidney-related mortality was estimated to 2.2 million annual deaths 4% of deaths worldwide [2]. To support renal patients, two methods are used: kidney transplantation and dialysis (hemodialysis and peritoneal dialysis). An estimated number of 1.4 million people worldwide need these treatments and this number is growing at 8% annually[3]. However, in hemodialysis, both patient's blood and dialysis fluid are pumped into the dialyzer in opposite directions to be purified based on the difference in the concentration of waste between both liquids [4].

Simulation and modeling became a well-established tool to assist health care decision-makers in evaluating systems design and knowing all technical design considerations to support decision-making, providing adequate information to physicians and managers, for forecasting and assistance in effective future planning [5]. Ciandrini et al. dealt with the modeling of potassium removing and the results showed how important to discuss the relationship among K+ apportionment between extracellular and intracellular compartments, and K concentration in the dialysate [6]. Annan et al.

suggested a model that takes into account the exchange of bicarbonate ions within the dialyzer and predicts the dynamics of dissolved exchange during the dialysis session, lasting 4 hours. This model was suggested to improve the acid-base status of patients with renal disease in its final stages by appropriate selection of HCO3− and electrolyte concentrations in dialysis fluid [7].

Maheshwari et al. modeled the dynamic balance between protein and toxins. The simulation indicated that the increase in the flow rate of the dialysis fluid increases the efficiency of detoxification, which is closely related to the protein, while the toxins that are not closely related, it is useful to increase the blood flow rate [8]. Dauda et al. developed a dialysis mathematical model in which the kidney was modeled using two departments. The model was validated using clinical data. They have found that dialysis twice a week with five hours per session is the optimal case to reduce the concertation of urea [9]. Kahshan et al. discussed blood filtration through a permeable membrane in a flat plate hemodialyzer (FPH). They built a mathematical model using Darcy's law, low Reynolds number, and long membrane length assumption, equations of motion. It also presented Casson fluid flow between two parallel permeable membranes with an application to the blood flow in (FPH) [10].

In this paper, a new expanded model is introduced which simulates the mechanisms of solutes and ions equilibrium and diffusion through the dialysis membrane, using the principles of mass transfer and diffusion using concentration differentiation. The results of this model will be primordial for the progress of our dialysis enhancement project relying on an electrophoresis principle to control the diffusion of ions substrates and the separation of blood toxins.

Methods

The present model consisted of three stages: 1- Modeling of diffusion process between the bloodstream and membrane dialyzing pipes. 2- Sodium, Potassium, and 3- Urea mass transferred inside the blood (in the extracellular space) during the dialysis process. In this research, solutes equilibrium equations are summarized in one generalized equation that can be applied for Na, K, and Urine. Three interconnected models were developed in MATLAB/Simulink environment. Finally, the results were compared with previous and related studies.

Diffusion process in dialysis

The dialyzer device is modeled as two centered pipes as shown in Fig. 1. The dialysate bath sketched as a container blue pipe with flow rate (Q_d), input concentration (C_{d_in}), and output concentration (C_{d_out}), the inner pipe referred to a blood vessel with the volumetric flow (Q_B), concentration value (C_{B_in}) in the input and (C_{B_out}) in the output.

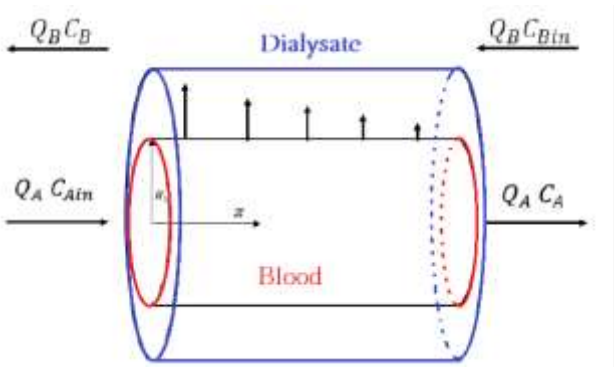

Figure 1. The Schematic of dialysis process

As hypothesis, the concentration of dialysate was equal to zero, since it is empty of toxins. According to the mass balance principle [11], and could apply the following equation referred to concentration differentiation depending on the mass transfer coefficient (k) [12]:

$$V_d \frac{dC_{d\_out}}{dt} = Q_d\left(C_{d\_in} - C_{d\_out}\right) - K\left(C_{d\_out} - C_{B\_out}\right) \quad 1$$

$$V_B \frac{dC_{B\_out}}{dt} = Q_B\left(C_{B\_in} - C_{B\_out}\right) + K\left(C_{d\_out} - C_{B\_out}\right) \quad 2$$

$$C_{d\_out}(0) = C_{d\_in} \qquad C_{B\_out}(0) = C_{B\_in} \quad 3$$

These equations briefly described the diffusion process between dialysate and blood depending on the concentration difference of urea between the two mediums. A Simulink model is proposed to simulates Eqs. 1-3, and plotted concentration variations according to mass transfer coefficient (K) as shown in Fig. 2.

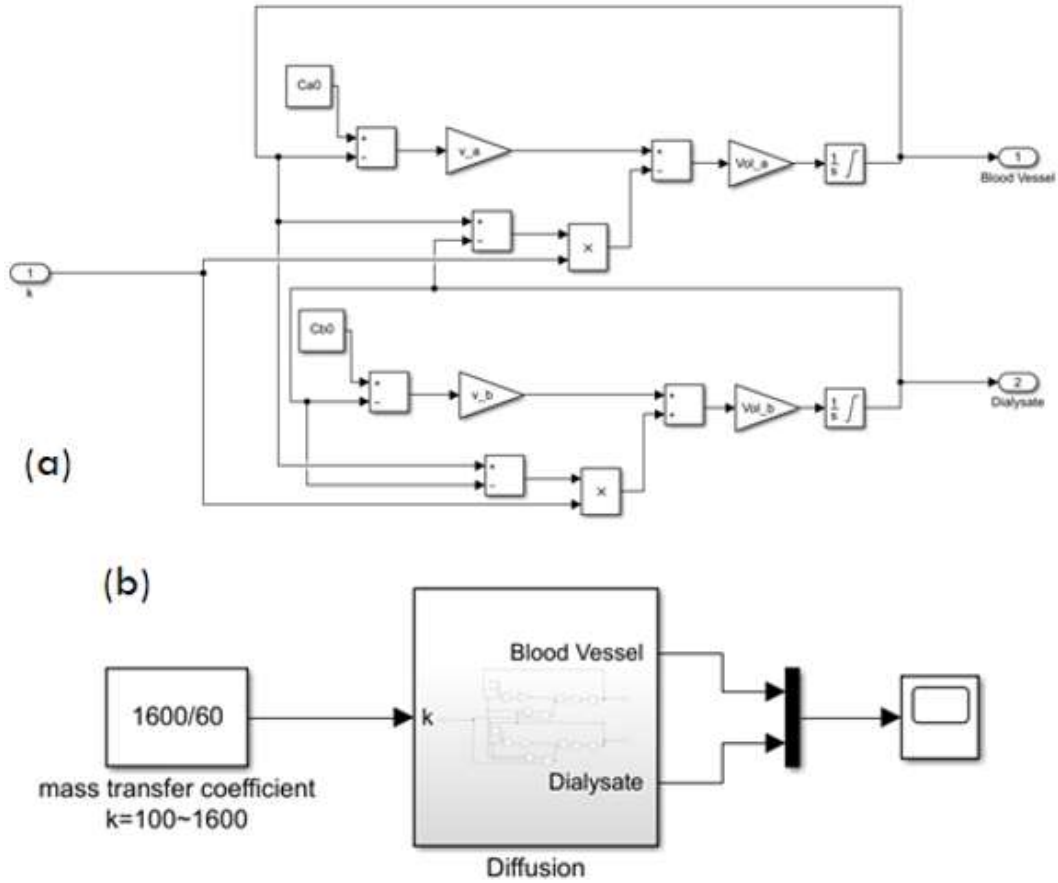

Figure. 2: MATLAB model of diffusion equations Eqs. 1, 2, 3. (a) The Renal model of the diffusion process, (b) Final embedded model with mass transfer coefficient input and the plotting of blood flow and dialysate.

Solutes mass transfer

This model part deal with mass balance equations describing the fluxes of each solute through the internal (IC) and external compartments (EC), and across dialyzer membrane. Baigent et al. summarized this process with one equation, which calculates sodium mass variations in EC according to sodium concentration in the dialysate and blood [13]. Ursino et al. published referential research in the field of electrolytes in the dialyzing process, with general equations that can be applied for Na, K, and Urea including their concentration changing in blood and dialysate [14]. Ciandrini et al. presented a model of potassium behavior within dialyzer, and they concluded the potassium flux out of the dialyzer QK, which was estimated as a function of the K+ concentration at the inlet (K_(k_d_in)) and outlet (K_(k_d_out)) dialysate. This actual paper uses the equations of potassium mass in the blood describing how potassium can be diffused between blood and dialysate.

As a result of combining the mathematical models related to the studies of Baigent and Ursino, an expanded equation that describes the behaviors of solutes has been concluded. Each gradient has different properties and considerations, but it was handled using simple initial conditions determined within Simulink models [6].

The equations below described the mass transfer equation, the change of solute in the blood entering the dialyzer, and EC concentration of solute. Those equations are modeled in MATLAB as shown in Fig. 4:

$$\frac{dM_{S_e}(t)}{dt} = D_S(C_{S_d}(t) - C_{S_e}(t) - U(t)C_{S_e}(t) = -(D_S + U(t))C_{S\_e}(t) + D_S C_{S\_d}(t) \quad 4$$

$$D_S = \frac{B(C_{S\_in}(t) - C_{S\_out}(t))}{(C_{S\_in}(t) - C_{S\_d}(t))} \quad 5$$

$$C_{S\_e} = \frac{M_{S\_e}(t)}{V_{ex}} \quad 6$$

Where:S: symbol refers to Na, K, and U.

D_S: *is the change of solute in solute content*

$M_S^e(t) = EC\ molar\ masses\ of\ solute$ $V_{ex} = Extracellular\ volume$

$C_{S\_e}(t) = EC\ concentration$ of solute $C_{S\_d}(t) =$ dialysate concentration of solute

$C_{S\_in}(t) =$
solute concentration of the blood entering dialysate.

$C_{S_{out}}(t)$
$=$ solute concentration of the blood leaving dialysate . $U(t) =$ ultrafiltration rate
$B(t) =$ blood flow rate at the dialyser inlet

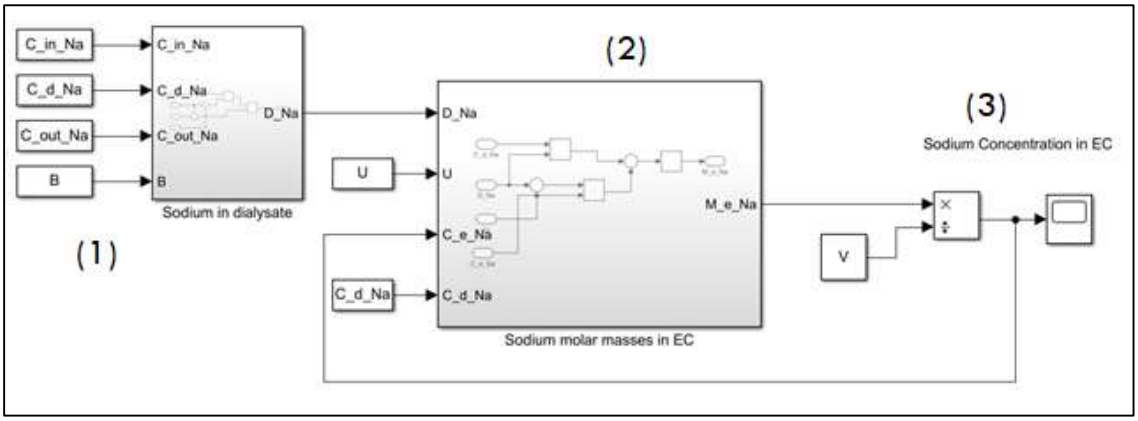

Figure 3. Subsystem models that describe Sodium solute behavior during dialyzing as described in Eq. 4,5,6. (1) Model of Sodium behavior in dialysate, (2) Sodium molar masses in EC model (3) Sodium concentration in EC after scaling to EC volume.

Results

After finishing the model implementation via Simulink, the simulation is conducted according to the parameters cited in Table 1, which used standards gradient concentrations in the blood and dialysate [15].

Fig. 4 illustrates the concentration change of blood and dialysate using the diffusion principle with different values of mass transfer coefficient (K). The most appropriate value of (K) equals to 700 which gave a good permeability. Fig. 5 shows the numerical variations of sodium and potassium and urea concentrations over the time.

Results validation was done by comparing the obtained values to relate and similar previous studies [13, 14, 6]. Table. 2, summarized the reference values in the actual study.

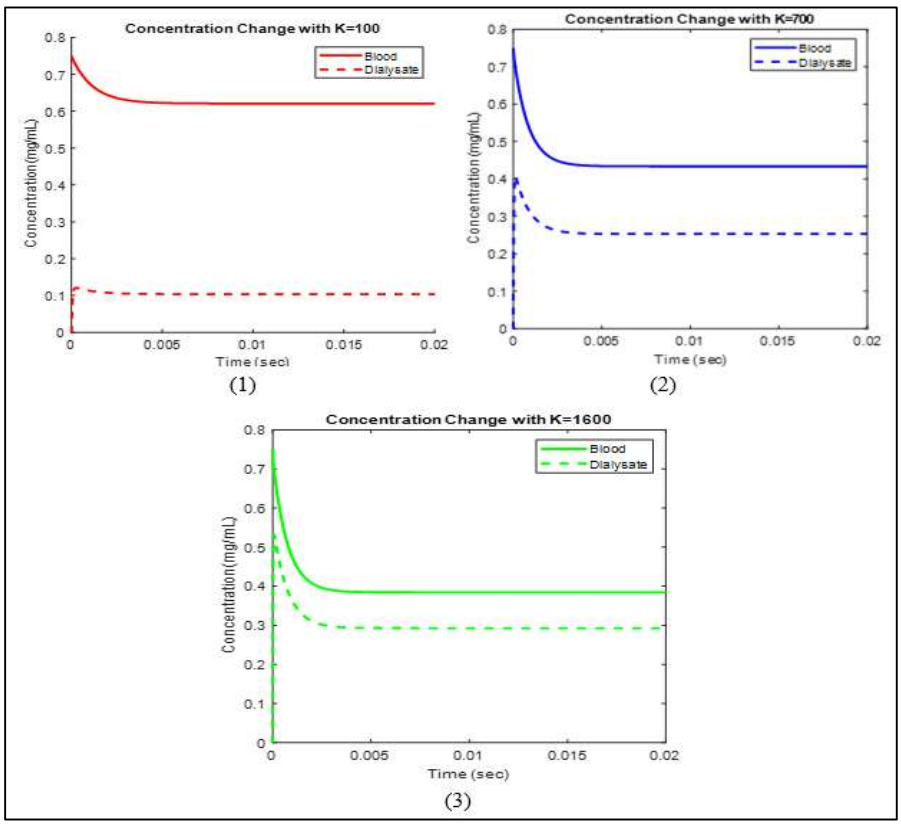

Figure 4. Diffusion results with different mass transfer coefficient values K = 100, 700, and 1600.

Table 1. Simulation parameters used in the actual model

parameter	Value	Units
Q_d	1	L/min
Q_B	0.3	L/min
C_{Na_in}, C_{Na_OUt}, C_{Na_d}	142, 140, 138	mmol/L
C_{K_in}, C_{K_OUt}, C_{K_d}	4.45, 2, 3.1	mmol/L
C_{U_in}, C_{U_OUt}, C_{U_d}	24, 0, 5	mmol/L

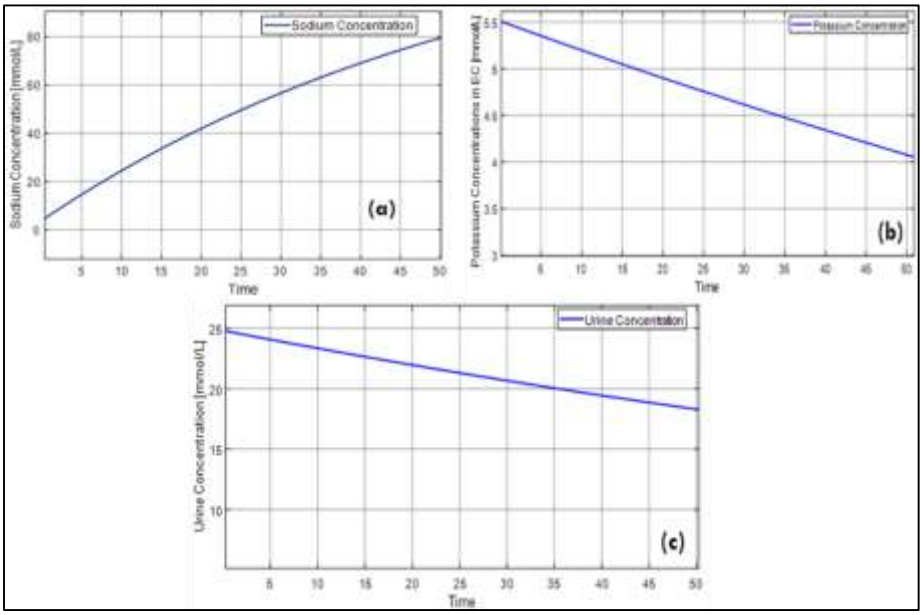

Figure 5. Simulation results of (a) Na, (b) K, and (c) Urine concentration variation.

Table. 2 showed the values of solutes concentration resulted of current model, compared to the regular values existed in the blood, and to the values of a previous related study [13].

Table 2. Comparison of ions concentrations

Solute	Blood	Baigent MODEL	ACTUAL model results	Units
Sodium	135 ~ 145	138	136.8	mmol/L
Potassium	3.5 ~ 5.1	3.7	2.186	mmol/L
Urea	7.1 ~ 8.3	9.1	7.34	mmol/L

As an additional step, the methods of diffusion modeling and solute concentrations in EC were combined by re-simulating the diffusion process and supposing that blood was composed of sodium solutes only. This was enabled in describing the behaviors of dialysate and Na blood concentrations inside both media as shown in Fig. 6.

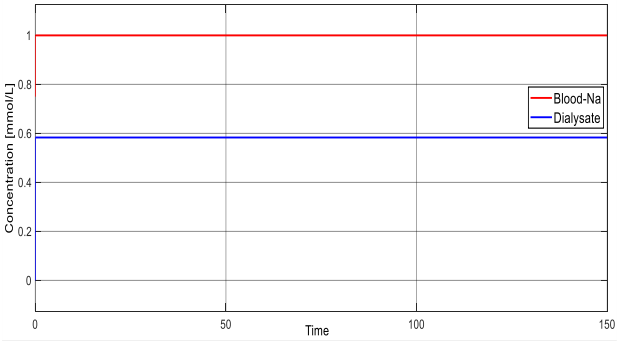

Figure 6. Diffusion results using dialysate and sodium based blood

Discussion:

Chronic kidney diseases are increasing worldwide with different symptoms and severity [16, 17]. The proposed model contained sub-models of electrolytes, in addition to the mass transfer model. The resutls of final model were validated by the values reported in the literature.

The final model presented a predictive system of cellular electrolytes (sodium, potassium, urea) and the pattern of plasma osmolarity. The final model's output of electrolytes concentrations in Table 2 using special parameters in Table. 1 showed reliable values of ions and predictable behavior of this model for any future aspects or modifications especially when we take about embedding electrophoresis with blood flow and mass transfer. The model results described the kinetics of solutes with small molecular weight, the fluid balance

between the extracellular and intracellular concentrations, and molecular balance.

Na+ balance (ECV balance) was an important task of any artificial kidney system.Na+ balance was on two criteria: dietary salt intake and Na+ removal during maintenance hemodialysis. The modeling of solutes kinetics totally based on reference [14], after enhancing the description of solutes kinetics during hemodiafiltration with new suggestions and validations. Coli et al. presented a contribution in the modeling of sodium concentration profile in the dialysate. Their work depended on an approximated estimation of the amount of sodium that is actually removed during hemodialysis [18].

Major differences with model that could not conduct a statistical study because of observations lack were the lack of the description of protein transport, and of parameters and the selection of coefficients values. Moreover, in the study, dialysis process is the repetition of passing blood process through the filter so that the percentages of salts, including sodium and potassium, as well as toxins, including urea and creatine, are reduced to levels below a certain level so that they remain within the limits of safety for the human body.

The present work can be emmbeded or expanded to involove some physiological changes in the human body like pregnant and preeclamptic women and

Conclusion:

The use of numerical modeling for renal function understanding seems to be very useful in producing the appropriate values for blood toxines elimination. Based on the models, the value of mass transfer coefficient could be determined, and the values of solutes could be predicted. It is recommended to use the actual model for the understanding of phenomena laying behind the ionic balance, and this information will be primordial for the development of implantable and bionic kidney which uses the principle of electrophoresis to separate between the ions and achieve the required and normal values, resulting in a more comfortable solution and prolonging the life of service of renal patients.

Authors' declaration:

- Conflicts of Interest: None.
  - We hereby confirm that all the Figures and Tables in the manuscript are original. Besides, the Figures and images, which are not, have been given the permission for re-publication attached with the manuscript.
- Authors sign on ethical consideration's approval.
- Ethical Clearance: The project was approved by the local ethical committee in Damascus University, Syria

Authors' contributions statement:

Conceptualization, S.M. and E.I.; methodology and investigation, S.M..; formal analysis, E.I., S.M., and A.D.; software, E.I.; writing—original draft preparation, S.M. and A.D.; writing—review and editing, E.I. and A.D..; supervision, A.D. and E.I. All authors have read and agreed to the published version of the manuscript.

Ethics Approval: The project was approved by the local ethical committee in Al Andalus University Hospital.

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النمذجة العددية للتوازن الأيوني الكلوي فيما يخص تطبيقات الكلى المزروعة

صالح مسعود [1] **أيهم درويش [1، 2]** **إبراهيم إسماعيل [3]**

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الخلاصة:

تعتبر الكلية البشرية من أهم أعضاء جسم الإنسان. تقوم بالعديد من الوظائف ولها تأثير كبير على عمل باقي الأعضاء. ومن أهم العلاجات الممكنة غسيل الكلى الذي يعمل ككلية صناعية خارجية، وقد عملت العديد من الدراسات على تعزيز آلية جريان الديالة وتحسين نفاذية غشاءها. تقدم هذه الدراسة نموذجاً رقمياً جديداً يعتمد على بحث سابق يناقش الاختلافات في تركيزات الصوديوم والبوتاسيوم وحمض البول في المنطقة خارج الخلية في الدم أثناء غسيل الكلى. تم في هذا البحث محاكاة المعادلات التفاضلية المتعلقة بالانتقال الكتلي وانتشارها وقمنا بتطوير النموذج في بيئة MATLAB Simulink. بدت قيمة 700 بأنها القيمة الأكثر ملاءمة لمعامل انتقال الكتلة، حيث حققت هذه القيمة أكبر نسبة لنفوذية الشوارد المدروسة. سمحت النماذج المطوَّرة في الدراسة الحالية بتتبع التغيرات الزمنية لتراكيز شوارد الصوديوم والبوتاسيوم والبولة، كما سمحت بتحديد زمن الوصول إلى القيم السريرية المذكورة في دراسات الأدب الطبي وذلك عند زمن 960 ms، وقد تمّ تقدير ذلك بمعدلات أخطاء لا تتجاوز 2% بالمقارنة مع قيم الدم الطبيعي للإنسان. يقدّم العمل الحالي تجربة أولية للجمع بين مبدأ النقل الشامل والانتشار لغسيل الكلى مع جهودنا في تصميم وتنفيذ كلية قابلة للزرع تعتمد على الرحلان الكهربي.

الكلمات المفتاحية: تطبيقات الكلى المزروعة، تصميم الكلى،ماتلاب، النمذجة العددية، توازن الأيونات الكلوية.